February 12, 1963

Dr. Gladys L. Hobby
Chas. Pfizer & Co., Inc.
630 Flushing Avenue
Brooklyn 6, New York

Dear Dr. Hobby:

May I refer to your paper in Science 97:205, 1943, concerning esters of penicillin?

We are still continually exploring new methods of selecting for various kinds of metabolically deficient mutants, and it recently occurred to me that we might look into esters, phosphates, and similar functional derivatives of potent antibiotics as selective agents that might be useful in the detection and isolation of bacterial mutants deficient in the hydrolytic enzyme that would release the free antibiotic. Your report on the benzohydryl ester of penicillin seemed to constitute an excellent starting point for verifying this notion, and I am writing to ask whether you have any further information on the antibacterial properties of this material subsequent to the 1943 paper.

Having so many free hydroxyl groups tetracycline would also seem to be an excellent candidate for forming derivatives, especially phosphates and other esters. If such materials have been prepared, and I must suppose that they have, I would be grateful for you for information on these as well. A further type of derivative in which we would be most interested would be a peptide.

If you can afford to furnish samples of any derivatives along these lines, I would be most grateful.

With best regards,

Sincerely yours,

Joshua Lederberg
Professor of Genetics

M. Joe Lien
Bacterial Labs, Syracuse

Hi, Joe:
The import of the above letter should be self-evident, and I am writing to you also to ask whether you may have some materials along these lines that we might be able to use. Most of our work at the present time is in Bacillus subtilis. What I am really looking forward to is the prospect of selecting for nuclease-deficient mutants by a similar method, but before embarking on what might be a fairly tricky synthesis of the appropriate nucleotide derivatives, it seemed worth while to try out the general procedure if we can obtain suitable compounds.

Best regards.